

Amendments to the Specification:

Please amend the specification by replacing the title as follows:

PORCINE CTLA-4 FOR XENOGRAFT-SPECIFIC IMMUNOSUPPRESSION BY
BLOCKING T-CELL CO-STIMULATION SIGNAL 2 (B7/CD28 INTERACTION)

Please amend the specification by replacing the abstract as follows:

The invention provides ~~means~~ compositions and methods for inhibiting T-cell mediated rejection of a xenotransplanted organ by blocking the delivery of co-stimulatory signal 2 (the B7/CD28 interaction) in order to prevent the activation of xenoreactive T-cells in the recipient. In a first aspect, co-stimulation is prevented by administration to the organ recipient of a soluble form of CTLA-4 from the xenogeneic donor organism. This preferentially binds B7 on the xenograft and blocks the interaction between B7 on the xenogeneic donor cells and CD28 on recipient T-cells. In a second aspect, co-stimulation is antagonised by expressing a ligand for CTLA-4 on the xenogeneic donor cells. This ligand binds to CTLA-4 on activated T-cells of the recipient and antagonises signal 2. In a third aspect, co-stimulation is prevented by expressing recipient organism MHC class II on the surface of the cells of the xenogeneic donor organ. The donor cells are thus able to present xenoantigens to a recipient T-cell in the context of self-MHC class II. If the donor cells do not express B7, or if B7 is blocked, the xenoreactive recipient T-cell becomes anergic.

Please amend the specification by inserting the following:

Page 12, line 21: The resulting 700bp fragment was sub-cloned into *EcoRI/HindIII* digested ~~pBluescript~~ PBLUESCRIPT®, and

Page 13, line 8: *HindIII/PstI* digested ~~pBluescript~~ PBLUESCRIPT®-IgG1 containing genomic DNA encoding intronic sequences

Page 13, line 12: The chimeric pCTLA4-Ig DNA sequence was released from ~~pBluescript~~ PBLUESCRIPT® as a *HindIII/BstXI*

Page 13, line 15: G418-resistant cells were separated using the ~~CaptureTec~~TM CAPTURETECTM system. These transfected cells

Page 14, line 18: (ii) quantitative characterisation of binding using ~~Biacore~~TM BIACORETM.

Page 15, line 10: resulting 113 base pair fragment was sub-cloned into *NotI/PstI* digested ~~pBluescript~~ PBLUESCRIPT®.

Page 15, line 12: *EcoRI/PstI* digested ~~pBluescript~~ PBLUESCRIPT®-IgG1, along with the *NotI/PstI* PCR product [Figure 12]. This

Page 15, line 25: *SalI/BamHI* fragment from ~~pBluescript~~ PBLUESCRIPT®-hCD8) into *EcoRI/BamHI* digested ~~pBluescript~~ PBLUESCRIPT®

Page 15, line 27: The *EcoRI/BamHI* fragment from ~~pBluescript~~ PBLUESCRIPT® was sub-cloned into the expression vector

Page 16, line 11: The resulting fragment was sub cloned into *HindIII/EcoRI* digested ~~pBluescript~~ PBLUESCRIPT® and the

Page 16, line 19: fragment was sub cloned into *HindIII/SalI* digested ~~pBluescript~~ PBLUESCRIPT® and sequenced.

Page 16, line 23: The resulting fragment was sub cloned into *HindIII/EcoRI* digested ~~pBluescript~~ PBLUESCRIPT® and the

Page 17, line 3: fragment was sub cloned into *HindIII/SalI* digested ~~pBluescript~~ PBLUESCRIPT® and called ~~pBluescript~~ PBLUESCRIPT®-hCD8.

Page 17, line 4: The extracellular domain of human CTLA-4 was cut from ~~pBluescript~~
PBLUESCRIPT® as an *EcoRI/SalI*

Page 17, line 6: ligated back into *EcoRI/BamHI* digested ~~pBluescript~~ PBLUESCRIPT®. The
whole CTLA-4-CD8 chimera was

Page 17, line 15: sFv-Ig fusion protein and soluble human CTLA4-Ig, using ~~Biacore™~~
BIACORE™